

this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Claims:

Please replace pending claims 299, 318, 339, 362, 373, 376, 381, 388, 391, 403, 404, 405, 415, 418, 430, 433, 445, 458, 475, 491, 494, 506, 517, 522, 534, 540, 552, 564, 579, 594, 607, 609, 610, 615, and 622 with the following claims 299, 318, 339, 362, 373, 376, 381, 388, 391, 403, 404, 405, 415, 418, 430, 433, 445, 458, 475, 491, 494, 506, 517, 522, 534, 540, 552, 564, 579, 594, 607, 609, 610, 615, and 622:

G¹
299. (Once Amended) A method of producing the polypeptide encoded by the polynucleotide of claim 287, comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide is expressed, and recovering said polypeptide.

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318. (Once Amended) A method of producing the polypeptide encoded by the polynucleotide of claim 305, comprising culturing a host cell comprising said

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polynucleotide under conditions such that said polypeptide is expressed, and recovering said polypeptide.

G3

339. (Once Amended) A method of producing the polypeptide encoded by the polynucleotide of claim 326, comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide is expressed, and recovering said polypeptide.

G4

362. (Once Amended) An isolated polynucleotide comprising a nucleic acid which encodes a polypeptide fragment at least 90% identical to amino acids 158 to 360 of SEQ ID NO:2; and

wherein a DR5 variant polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 158-360 of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

G5

373. (Once Amended) A method of producing the polypeptide fragment encoded by the polynucleotide of claim 362, comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide fragment is expressed, and recovering said polypeptide fragment.

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376. (Once Amended) The polynucleotide of claim 374, wherein said first nucleic acid encodes a polypeptide fragment; and wherein a DR5 variant polypeptide

consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids
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158-360 of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment,
induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

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381. (Once Amended) A method of producing a vector that comprises
inserting the polynucleotide of claim 374 into a vector.

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388. (Once Amended) A method of producing the polypeptide fragment
encoded by the polynucleotide of claim 376, comprising culturing a host cell comprising
said polynucleotide under conditions such that said polypeptide fragment is expressed,
and recovering said polypeptide fragment.

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391. (Once Amended) The polynucleotide of claim 389, which encodes a
polypeptide fragment, wherein a DR5 polypeptide consisting of amino acids 1 to 360 of
SEQ ID NO:2, with the exception that amino acids 158-360 of SEQ ID NO:2 are deleted
and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-
expressed in human breast carcinoma cells.

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403. (Once Amended) A method of producing the polypeptide fragment
encoded by the polynucleotide of claim 391, comprising culturing a host cell comprising
said polynucleotide under conditions such that said polypeptide fragment is expressed,
and recovering said polypeptide fragment.

404. (Once Amended) An isolated polynucleotide comprising a nucleic acid which encodes a polypeptide fragment at least 90% identical to amino acids 273 to 340 of SEQ ID NO:2;

wherein a DR5 variant polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 273-340 of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

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405. (Once Amended) The polynucleotide of claim 404, wherein said polypeptide fragment is at least 95% identical to amino acids 273 to 340 of SEQ ID NO:2.

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415. (Once Amended) A method of producing the polypeptide fragment encoded by the polynucleotide of claim 404, comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide fragment is expressed, and recovering said polypeptide fragment.

G 12

418. (Once Amended) The polynucleotide of claim 416, wherein said first nucleic acid encodes a polypeptide fragment, and wherein a DR5 variant polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 273-340 of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

430. (Once Amended) A method of producing the polypeptide fragment

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encoded by the polynucleotide of claim 418, comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide fragment is expressed, and recovering said polypeptide fragment.

433. (Once Amended) The polynucleotide of claim 431, wherein said nucleic

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acid encodes a polypeptide fragment, and wherein a DR5 polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 273-340 of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

445. (Once Amended) A method of producing the polypeptide fragment

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encoded by the polynucleotide of claim 433, comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide fragment is expressed, and recovering said polypeptide fragment.

458. (Once Amended) A method of producing the polypeptide encoded by the

G¹⁶
polynucleotide of claim 446 comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide is expressed, and recovering said polypeptide.

475. (Once Amended) A method of producing the polypeptide encoded by the

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polynucleotide of claim 462 comprising culturing a host cell comprising said

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polynucleotide under conditions such that said polypeptide is expressed, and recovering
said polypeptide.

G 18

491. (Once Amended) A method of producing the polypeptide encoded by the
polynucleotide of claim 476 comprising culturing a host cell comprising said
polynucleotide under conditions such that said polypeptide is expressed, and recovering
said polypeptide.

G 19

494. (Once Amended) The polynucleotide of claim 492, which encodes a
polypeptide fragment, wherein a DR5 polypeptide consisting of amino acids 1 to 360 of
SEQ ID NO:2, with the exception that the amino acids encoded by said 30 contiguous
amino acids are deleted and replaced with said polypeptide fragment, induces apoptosis
in vitro when over-expressed in human breast carcinoma cells.

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506. (Once Amended) A method of producing the polypeptide encoded by the
polynucleotide of claim 492 comprising culturing a host cell comprising said
polynucleotide under conditions such that said polypeptide is expressed, and recovering
said polypeptide.

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517. (Once Amended) A method of producing a polypeptide comprising the at
least 50 contiguous amino acids encoded by the polynucleotide of claim 507 comprising

G²¹
G_{Cont} culturing a host cell comprising said polynucleotide under conditions such that said polypeptide is expressed, and recovering said polypeptide.

522. (Once Amended) The polynucleotide of claim 518, which hybridizes to the complement of nucleotides 754 to 1362 of SEQ ID NO:1, and which encodes a polypeptide fragment, wherein a DR5 variant polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 158-360 of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

G²²
G²³ 534. (Once Amended) A method of producing the polypeptide fragment encoded by the polynucleotide of claim 522 comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide fragment is expressed, and recovering said polypeptide fragment.

G²⁴ 540. (Once Amended) The polynucleotide of claim 535, wherein said first nucleic acid encodes a polypeptide fragment, and wherein a DR5 variant polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 158 to 360 of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

G²⁵ 552. (Once Amended) A method of producing the polypeptide fragment encoded by the polynucleotide of claim 540 comprising culturing a host cell comprising

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said polynucleotide under conditions such that said polypeptide fragment is expressed,
and recovering said polypeptide fragment.

G²⁶
564. (Once Amended) A method of producing the polypeptide encoded by the
polynucleotide of claim 553 comprising culturing a host cell comprising said
polynucleotide under conditions such that said polypeptide is expressed, and recovering
said polypeptide.

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579. (Once Amended) A method of producing a polypeptide comprising the
amino acids encoded by the polynucleotide of claim 565, comprising culturing a host cell
comprising said polynucleotide under conditions such that said polypeptide is expressed,
and recovering said polypeptide.

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594. (Once Amended) A method of producing the protein encoded by the
polynucleotide of claim 580 comprising culturing a host cell comprising said
polynucleotide under conditions such that said protein is expressed, and recovering said
protein.

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607. (Once Amended) A method of producing the polypeptide encoded by the
polynucleotide of claim 595 comprising culturing a host cell comprising said
polynucleotide under conditions such that said polypeptide is expressed, and recovering
said polypeptide.

609. (Once Amended) The polynucleotide of claim 608, wherein a DR5 variant polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that 50 contiguous amino acids of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, binds TRAIL.

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610. (Once Amended) The polynucleotide of claim 608, wherein a DR5 variant polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that 50 contiguous amino acids of SEQ ID NO:2 are deleted and replaced with said polypeptide fragment, induces apoptosis *in vitro* when over-expressed in human breast carcinoma cells.

G³¹

615. (Once Amended) A method of producing a vector that comprises inserting the polynucleotide of claim 608 into a vector.

G³²

622. (Once Amended) A method of producing the polypeptide fragment encoded by the polynucleotide of claim 608 comprising culturing a host cell comprising said polynucleotide under conditions such that said polypeptide fragment is expressed, and recovering said polypeptide fragment, wherein said polypeptide fragment binds an antibody with specificity for a polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2.